

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte DOUGLAS HOVEY, TUULA RYDE, and H. WILLIAM BOSCH

Appeal 2011-001850
Application 10/768,194
Technology Center 1600

Before LORA M. GREEN, MELANIE L. McCOLLUM, and
STEPHEN WALSH, *Administrative Patent Judges*.

WALSH, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) involving claims to a sterile filterable fluticasone dispersion, a composition, a method of making the composition, and a method of treating a subject with the composition. The Patent Examiner rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 17, 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 are on appeal. Claim 17 is representative and reads as follows:

17. A sterile filterable dispersion comprising:
- (a) an aqueous dispersion medium;
 - (b) fluticasone particles sufficiently small to pass through a 0.2 μ m filter, and have a phase selected from the group consisting of a crystalline phase, an amorphous phase, and a semi-crystalline phase; and
 - (c) at least one surface stabilizer adsorbed on the surface of the fluticasone particles, wherein the dispersion is sterilized by filtration through a 0.2 μ m filter.

The Examiner rejected the claims as follows:

- claims 17, 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 under 35 U.S.C. § 103(a) as unpatentable over Wiedmann¹ and Saidi;² and
- claims 17, 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 under 35 U.S.C. § 103(a) as unpatentable over Wood,³ Saidi, and Biggadike.⁴

For each rejection, claims 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 have not been argued separately and therefore stand or fall with claim 17. 37 C.F.R. § 41.37(c)(1)(vii).

¹ US Patent No. 5,747,001 issued to Timothy S. Wiedmann et al., May 5, 1998.

² US Patent No. 6,241,969 issued to Zahir Saidi et al., Jun. 5, 2001.

³ Patent Application Publication No. WO 96/25918 by Ray W. Wood et al., published Aug. 29, 1996.

⁴ Patent Application Publication No. US 2003/0073676 A1 by Keith Biggadike et al., published Apr. 17, 2003.

OBVIOUSNESS

The Issues

The rejection over Wiedmann and Saidi

The Examiner's position is that Wiedmann taught an aerosol comprising droplets of an aqueous dispersion of nanoparticles comprising insoluble beclomethasone particles having a surface modifier on its surface. (Ans. 4.) The Examiner found that Wiedmann also disclosed a method of making the aerosol and methods for treating respiratory conditions using the aerosol. (*Id.* at 4-5.) The Examiner also found that Wiedmann taught using tyloxapol as a preferred surface modifier. (*Id.* at 5.) The Examiner found that Wiedmann taught various methods of forming the desired nanoparticle dispersion, including the use of microprecipitation which produced a dispersion of beclomethasone having an average particle size of less than 400 nm. (*Id.* at 6.) The Examiner found that Wiedmann disclosed preferred embodiments wherein the effective average particle size was less than about 300 nm and more preferably less than about 250 nm. (*Id.* at 7.) For some embodiments, Wiedmann disclosed achieving an effective average particle size of less than about 100 nm. (*Id.*) However, the Examiner found that Wiedmann differed from the instantly claimed invention by not teaching the use of fluticasone particles or sterile filtration. (*Id.*)

The Examiner found that Saidi taught compositions comprising corticosteroid compounds, in particular beclomethasone and fluticasone, formulated with a surfactant component. (*Id.*) The Examiner found that Saidi sterilized the composition by passing it through a 0.22 micron sterile filter. (*Id.* at 8.)

According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Wiedmann and Saidi to yield the claimed invention. (*Id.*) The Examiner reasoned that a skilled artisan would have been motivated to use fluticasone in Wiedmann's formulation with a reasonable expectation of success because Saidi suggested that fluticasone and beclomethasone are functionally equivalent glucocorticosteroids in the treatment of respiratory illnesses. (*Id.*)

According to the Examiner, it would have also been obvious to use Saidi's sterile filtration technique in Wiedmann's formulation and process because Wiedmann also taught filtration of its active agent/tyloxapol nanoparticles. (*Id.* at 9.) The Examiner reasoned that a skilled artisan would have been motivated to implement Saidi's sterile filtration in place of Wiedmann's simple filtration because sterilization of formulations is beneficial to recipients. (*Id.*)

The rejection over Wood, Saidi, and Biggadeke

The Examiner found that Wood taught an aerosol comprising droplets of an aqueous dispersion of nanoparticles comprising insoluble particles of an active agent, including corticosteroids such as beclomethasone, having a surface modifier, such as tyloxapol, on the surface. (Ans. 10-11.) The Examiner also found that Wood taught a method of treating respiratory conditions comprising the steps of forming the aerosol and administering it to a mammal in need of such treatment. (*Id.* at 10.) Additionally, the Examiner found that Wood taught applying a mechanical means to reduce the particle size of the therapeutic agent to an effective average particle size of less than about 400 nm. (*Id.* at 11.) However, the Examiner found that

Wood differed from the instantly claimed invention by not teaching fluticasone particles or sterile filtration. (*Id.*)

The Examiner relied on Saidi for the same reasons discussed regarding the combination of Wiedmann and Saidi. (*Id.*)

Further, the Examiner found that Biggadike taught pharmaceutical formulations comprising an aqueous carrier liquid having dissolved fluticasone and a solubilizing agent. (*Id.*) The Examiner found that Biggadike taught that the solubility of fluticasone esters can be increased by dissolution in an aqueous carrier liquid of hydroxyl containing organic co-solvating agent or of phosphatidyl choline. (*Id.*) Additionally, the Examiner found that Biggadike taught that a preferred surfactant for use as the solubilizing agent was tyloxapol. (*Id.* at 12.) The Examiner found that Biggadike taught that its formulations may be employed in various routes of administration, including by inhalation for the treatment of conditions including respiratory illnesses. (*Id.*)

According to the Examiner, it would have been obvious to combine the prior art teachings. The Examiner found that a skilled artisan would have been motivated to use fluticasone instead of beclomethasone in Wood's formulation because Saidi taught that both corticosteroids are preferred compounds in treating respiratory illnesses. Therefore, the Examiner reasoned that the artisan would have had a reasonable expectation of successfully using fluticasone because the two agents are functionally equivalent glucocorticosteroids. (*Id.* at 13.)

According to the Examiner, it would also have been obvious to use Saidi's sterile filtration technique in the formulations and process of Wood because Wood taught a filtration of nanoparticles of beclomethasone and

tyloxapol. (*Id.*) The Examiner reasoned that the artisan would have been motivated to implement sterile filtration in place of a simple filtration because sterilization of formulations further benefits the recipients. (*Id.*)

Appellants' Contentions

Appellants contend that “[t]here is no teaching or suggestion that Wiedmann’s aerosol composition can be sterilized filtering through a 0.2 µm filter.” (App. Br. 10.) According to Appellants, “sterile filtration can be difficult for aerosol formulations of nanoparticulate drugs due to the required small particle size of the composition.” (*Id.* at 11.) Further, Appellants assert that a skilled artisan would not have applied Saidi’s sterile filtration technique to Wiedmann’s composition because Saidi’s method required the active agent to be *dissolved* in a surfactant before passing it through a 0.22 micron filter. (*Id.*) In contrast, Wiedmann and the claimed invention are directed to dispersions. (*Id.*) According to Appellants, a skilled artisan “would have understood that solutions can easily pass a 0.22 micron filter while a dispersion may cause the filter to clog if the particles in the dispersion [are] not sufficiently small.” (*Id.*)

Appellants also contend that Wiedmann’s filtration amounted to a separation technique to separate larger particles from smaller particles or solids from liquid, rather than a sterilization technique to remove microorganisms as disclosed by Saidi. (*Id.* at 12.) Therefore, Appellants assert that a skilled artisan would not have been motivated to implement Saidi’s sterile filtration in place of Wiedmann’s simple filtration. (*Id.*)

Regarding the rejection over Wood, Saidi, and Biggadike, Appellants assert that “the rejection rationale is essentially the same as that of the rejection based on Wiedmann and Saidi. Thus, the arguments in the

foregoing section are incorporated by reference.” (*Id.*) Specifically, Appellants assert that “[t]here is neither evidence that Wood’s aerosol compositions are suitable for sterile filtration nor an indication that Saidi’s sterile filtration technique can be applied to Wood’s compositions.” (*Id.* at 13.) According to Appellants, Wood’s filtration amounted to a separation technique and did not suggest sterile filtration. (*Id.*)

Appellants further assert that “Biggadike fails to address the deficiencies of Wood and Saidi....” (*Id.*) Appellants also assert that the Examiner has not established “why one skilled in the art would have any reason to select tyloxapol as a surface stabilizer in the claimed invention, which adsorbs on the surface of fluticasone particles to prevent agglomeration or aggregation, in view of Biggadike’s teaching of using tyloxapol as a [sic. solubilizer].” (*Id.*)

The issue with respect to these rejections is whether the record supports the Examiner’s conclusion that the cited references would have made the claimed invention obvious.

Findings of Fact

1. We agree with the Examiner’s explicit findings regarding the scope and content of the prior art references. (*See* Ans. 3-13.)
2. Wood disclosed that tyloxapol “may function as a surface modifier, as a stabilizer, and/or as a dispersant.” (Wood 8, ll. 8-9.)

Principles of Law

It is well-established that a conclusion that the claimed subject matter is *prima facie* obvious must be supported by evidence, as shown by some

objective teaching in the prior art or by knowledge generally available to one of ordinary skill in the art that would have led that individual to combine the relevant teachings of the references to arrive at the claimed invention. *See In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988).

“The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). “If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability.” *Id.* at 417.

“Obviousness does not require absolute predictability of success...*all that is required is a reasonable expectation of success.*” *In re Kubin*, 561 F.3d 1351, 1360 (Fed. Cir. 2009).

Analysis

The rejection over Wiedmann and Saidi

We are not persuaded by Appellants’ contentions that Wiedmann did not suggest that its aerosol could be sterilized by filtration through a 0.2 µm filter, or that a skilled artisan would not have applied Saidi’s sterile filtration technique to Wiedmann’s dispersion. (App. Br. 10-11.) In rejecting the claims (Ans. 4-9) the Examiner relied on the combined teachings of the prior art, along with the knowledge generally known in the art at the time of the invention as providing the suggestion and motivation for sterilizing Wiedmann’s aerosol dispersion by filtration through a 0.2 micron filter. *See Fine*, 837 F.2d at 1074. As the Examiner explained, Wiedmann disclosed that its beclomethasone dispersion may comprise particles that are smaller than this filter. (Ans. 7.) Saidi disclosed sterilizing its composition,

comprising beclomethasone or fluticasone, by passing it through a 0.22 micron filter. (*Id.* at 8.) The Examiner explained that an artisan would have been motivated to sterilize Wiedmann's dispersion according to the technique disclosed in Saidi because sterilization of a formulation provides additional benefits to its recipients. (*Id.* at 9.) We agree. The Examiner's rejection merely involved combining familiar elements according to known methods that yielded a predictable result. *See KSR Int'l Co.*, 550 U.S. at 416.

To the extent that Wiedmann's dispersion comprised particles that were not smaller than a 0.2 micron filter, a skilled artisan would have known that such particle size needed to be reduced before passing them through Saidi's filter. Appellants acknowledged this fact by asserting that a skilled artisan "would have understood that ... a dispersion may cause the filter to clog *if the particles in the dispersion [are] not sufficiently small.*" (App. Br. 11, emphasis added.) Reducing the size of the particles was within the skill of the artisan, as evidenced by Wiedmann's disclosure. (*See* Ans. 6-7.) Therefore, the Examiner's combination involved implementing a predictable variation that was within the skill in the art. *See KSR Int'l Co.*, 550 U.S. at 417.

We agree with the Examiner that a skilled artisan would have used Saidi's filtration technique on a dispersion. As Appellants' acknowledged, a skilled artisan would have considered the size of the particles to determine if sterile filtration would work, not merely whether the particles were formulated as a solution or dispersion. We do not agree that Appellants have provided evidence that a skilled artisan would not have had at least a reasonable expectation of success in combining the teachings of Wiedmann

and Saidi based upon the prior art and knowledge generally available in the art at the time of the invention. *Kubin*, 561 F.3d at 1360 (obviousness requires a *reasonable* expectation of success- not absolute predictability).

Appellants also assert that a skilled artisan would not have been motivated to implement Saidi's filtration in place of Wiedmann's simple filtration because Saidi's technique removed microorganisms. (App. Br. 12.) This argument is also unpersuasive. The Examiner articulated sound reasoning (Ans. 9) showing a prior art known motivation to combine Saidi's filtration with Wiedmann's aerosol: providing sterilization was a known benefit to the recipient of treatment. *See In re Kahn*, 441 F.3d 977, 989 (Fed. Cir. 2006) (motivation to combine need only be supported by an articulated reasoning with rational underpinnings).

Accordingly, we affirm the Examiner's rejection over Wiedmann and Saidi.

The rejection over Wood, Saidi, and Biggadeke

We are not persuaded by Appellants' contention that "[t]here is neither evidence that Wood's aerosol compositions are suitable for sterile filtration nor an indication that Saidi's sterile filtration technique can be applied to Wood's compositions." (See App. Br. 13.)

As discussed regarding the first rejection, the Examiner relied on the teaching of the combined prior art, along with the knowledge generally available to the skilled artisan at the time of the invention for the suggestion to sterilize Wood's aerosol using Saidi's filtration technique. (Ans. 10-13.)

As the Examiner explained, Wood disclosed that its beclomethasone dispersion may comprise particles having an effective average particle size of less than about 400 nm. (*Id.* at 11.) The Examiner found that Saidi

disclosed sterilizing its composition, comprising beclomethasone or fluticasone, by passing it through a 0.22 micron filter. (*Id.* at 8.) The Examiner explained that an artisan would have been motivated to sterilize Wood's dispersion according to the technique disclosed in Saidi because sterilization of a formulation provides additional benefits to its recipients. (*Id.* at 9.) We agree. The Examiner's rejection merely involved combining familiar elements according to known methods that yielded a predictable result. *See KSR Int'l Co.*, 550 U.S. at 416.

Moreover, to the extent that Wood disclosed dispersions comprising particles that were not smaller than a 0.2 micron filter, a skilled artisan would have known that such particle size needed to be reduced before passing them through Saidi's filter. Appellants acknowledged this fact by asserting that a skilled artisan "would have understood that ... a dispersion may cause the filter to clog *if the particles in the dispersion [are] not sufficiently small.*" (App. Br. 11, emphasis added.) Selecting smaller particles was within the skill of the artisan, as evidenced by Wood's disclosure of particle sizes less than about 100 nm. (*See* Ans. 17.) The evidence demonstrates that the Examiner's combination involved implementing a predictable variation that was within the skill in the art. *See KSR Int'l Co.*, 550 U.S. at 417.

Appellants also assert that "Wood has no suggestion whatsoever to sterile filter the composition." (App. Br. 13.) This argument is also unpersuasive. As discussed, the Examiner articulated sound reasoning for combining Saidi's sterile filtration with Wood's aerosol, that is, to provide a sterilized formulation with a known benefit to the treatment recipient. *See In*

re Kahn, 441 F.3d 977, 989 (Fed. Cir. 2006) (motivation to combine need only be supported by an articulated reasoning with rational underpinnings).

Appellants further assert that the Examiner has not established “why one skilled in the art would have any reason to select tyloxapol as a surface stabilizer in the claimed invention, which adsorbs on the surface of fluticasone particles to prevent agglomeration or aggregation, in view of Biggadike’s teaching of using tyloxapol as a solubilizer.” (*Id.*) This argument is not persuasive because Wood, the primary reference, disclosed using tyloxapol as a particularly preferred surface modifier and further disclosed that it may function as a surface modifier, as a stabilizer, and/or as a dispersant. (FF-2; *see also* Ans. 19.)

Accordingly, we affirm the Examiner’s rejection over Wood, Saidi and Biggadike.

CONCLUSION OF LAW

The record supports the Examiner’s conclusion that the cited references would have made the claimed invention obvious.

SUMMARY

We affirm the rejection of claims 17, 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 under 35 U.S.C. § 103(a) as unpatentable over Wiedmann and Saidi; and

we affirm the rejection of claims 17, 19-24, 28-44, 47, 49-61, 64-67, 69, and 71-81 under 35 U.S.C. § 103(a) as unpatentable over Wood, Saidi, and Biggadike.

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No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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